15

20

## **CLAIMS**

## We claim:

5

- 1. A targeting construct comprising:
  - (a) a first polynucleotide sequence homologous to a tryptase gene;
  - (b) a sedond polynucleotide sequence homologous to the tryptase gene; and
  - (c) a selectable marker.
- 2. The tryptase targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
- 10 3. A method of producing a targeting construct, the method comprising:
  - (a) providing a first polynucleotide sequence homologous to a tryptase gene;
  - (b) providing a second polynucleotide sequence homologous to the tryptase;
  - (c) providing a selectable marker; and
  - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the tryptase targeting construct.
  - 4. A method of producing a targeting construct, the method comprising:
    - (a) providing a polynucleotide comprising a first sequence homologous to a first region of a tryptase gene and a second sequence homologous to a tryptase gene;
    - (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct
  - 5. A cell comprising a disruption in a tryptase gene.
  - 6. The cell of claim 5, wherein the cell is a murine cell.
  - 7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
  - 8. A non-human transgenic animal comprising a disruption in a tryptase gene.
- 25 9. A cell derived from the non-human transgenic animal of claim 8.
  - 10. A method of producing a transgenic mouse comprising a disruption in a tryptase gene, the method comprising:
    - (a) introducing the targeting construct of claim 1 into a cell;
    - (b) introducing the cell into a blastocyst;
- 30 (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

5

10

15

20

25

- (d) breeding the chimeric mouse to produce the transgenic mouse.
  11. A method of identifying an agent that modulates the expression of a tryptase, the method comprising:

  (a) providing a non-human transgenic animal comprising a disruption in a tryptase gene;
  (b) administering an agent to the non-human transgenic animal; and
  (c) determining whether the expression of tryptase in the non-human transgenic
- 12. A method of identifying an agent that modulates the function of a tryptase, the method comprising:
  - (a) providing a non-human transgenic animal comprising a disruption in a tryptase gene;
  - (b) administering an agent to the non-human transgenic animal; and
  - (c) determining whether the function of the disrupted tryptase gene in the non-human transgenic animal is modulated.
- 13. A method of identifying an agent that modulates the expression of tryptase, the method comprising:
  - (a) providing a cell comprising a distruption in a tryptase gene;
  - (b) contacting the cell with an agent; and

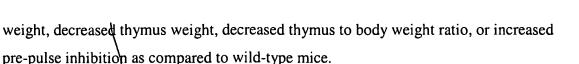
animal is modulated.

- (c) determining whether expression of the tryptase is modulated.
- 14. A method of identifying an agent that modulates the function of a tryptase gene, the method comprising:
  - (a) providing a cell comprising a disruption in a tryptase gene;
  - (b) contacting the cell with an agent; and
  - (c) determining whether the function of the tryptase gene is modulated.
- 15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.
- 16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.
- 17. A transgenic mouse comprising of distuption in a tryptase gene, wherein the
- 30 transgenic mouse exhibits at least one of the following phenotypes: decreased body

10

15

20



- 18. The transgenic mouse of claim 17, wherein the body weight is a decrease of 20 % in female transgenic mice as compared to female wild-type mice.
- 5 19. The transgenic mouse of claim 17, wherein the body weight is a decrease of 15% in female transgenic mice as compared to female wild-type mice.
  - 20. A method of producing a transgenic mouse comprising a disruption in a tryptase gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: decreased body weight, decreased thymus weight, decreased thymus to body weight ratio, or increased pre-pulse inhibition as compared to wild-type mice, the method comprising:
    - (a) introducing a tryptase gene targeting construct into a cell;
    - (b) introducing the cell into a blastocyst;
    - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse/gives birth to a chimeric mouse; and
    - (d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a tryptase gene.
  - 21. A cell derived from the transgenic mouse of claim 17 or claim 20.
  - 22. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a tryptase gene, the method comprising:
    - (a) administering an agent to a transgenic mouse comprising a disruption in a tryptase gene; and
  - (b) determining whether the agent ameliorates at least one of the following phenotypes: decreased body weight, decreased thymus weight, decreased thymus to body weight ratio, or increased pre-pulse inhibition as compared to wild-type mice.
- 25 23. An agent identified by the method of claim 20 or claim 21.

ADD